TYSABRI® RISK MINIMIZATION ACTION PLAN: SUMMARY OF TOUCH™

TOUCH™ is a distribution program designed to assess the risk of progressive multifocal leukoencephalopathy (PML) associated with TYSABRI®, minimize the risk of PML, minimize death and disability due to PML, and promote informed risk-benefit decisions regarding TYSABRI® use. The risks of TYSABRI® treatment are addressed through the distribution program, along with education of prescribers, pharmacists, infusion center staff, and patients about potential PML infection associated with TYSABRI® treatment.

1. Prescribing Program

1.1 General Requirements

Biogen Idec, Inc. will ensure that the following requirements are addressed by its Risk Minimization Action Plan, TOUCH™:

- TYSABRI® will only be available under a special restricted distribution program called TOUCH™.
- Only prescribers registered with TOUCH™ and who agree to comply with the TOUCH™ program will be able to prescribe TYSABRI®.
- Only infusion centers registered and authorized under TOUCH™ will be able to administer TYSABRI®.
- Only pharmacies registered with TOUCH™ will be able to dispense TYSABRI® to affiliated authorized infusion centers.
- Only patients enrolled in TOUCH™ and who agree to comply with the TOUCH™ program will be able to receive TYSABRI®.
- All TOUCH™ prescribers, pharmacies, infusion centers, and patients will be educated about the TOUCH™ program and the risks of TYSABRI® treatment.
- Safety surveillance, including monitoring and reporting of PML infections, other serious opportunistic infections, and deaths and systematic tracking of patients and drug disposition will be conducted.

1.2 Pharmacy and Infusion Center Requirements

Biogen Idec, Inc. will limit the distribution of TYSABRI® through specialty and central pharmacies to authorized infusion centers. The agreements between Biogen Idec and the specialty and central pharmacies and infusion centers require the following:

- All pharmacies and infusion sites will be registered with the TOUCH™ program, and agree to comply with the TOUCH™ program.

- Infusion sites and central pharmacies will obtain TYSABRI® directly from a single contract distributor or specialty pharmacy.

- All appropriate pharmacy and infusion center staff will be trained by Biogen Idec and/or Elan Pharmaceuticals about the TOUCH™ program and about the known risks, potential benefits, and appropriate use of TYSABRI®.

- All appropriate pharmacy and infusion center staff will be trained by Biogen Idec and/or Elan Pharmaceuticals in adverse experience reporting procedures, including 15 day reporting of PML infection, other serious opportunistic infections, and deaths.

- Infusion center staff are to follow the infusion guidelines outlined below:

    - Accept only prescriptions from prescribers in the TOUCH™ program.
    - Only infuse patients who are enrolled in the TOUCH™ program.
    - Prior to infusing a patient, the infusion site will verify in the patient's medical record that the patient is authorized to receive TYSABRI®.
    - Prior to infusing a patient, the infusion site will, confirm that there is a current Notice of Patient Authorization on file, and confirm that there is not a Notice of Discontinuation on file.
    - Prior to infusing a patient, the infusion site will provide the patient the Medication Guide and give the patient time to read it.
    - Prior to infusing a patient, the infusion site will complete the Pre-Infusion Patient Checklist and confirm prescriber clearance if needed.
    - Within one day of completing the Pre-Infusion Patient Checklist, the infusion site will fax the form to Biogen Idec.
    - The infusion site will not dispense TYSABRI® if it is determined that the patient (or their prescriber) is not in conformance with the TOUCH™ program.
    - Keep a record of the TYSABRI® prescription, Notice of Patient Authorization, and the Pre-infusion Patient Checklist, with each TYSABRI® prescription for each corresponding patient.

- Central pharmacies are to follow the dispensing guidelines outlined below:

    - Fill valid prescriptions for TYSABRI® in accordance with all applicable laws and regulations
    - Dispense TYSABRI® only to affiliated authorized infusion sites.

- Complete the TYSABRI® Inventory Tracking Log for every dose/vial of TYSABRI® dispensed to authorized infusion sites. The Inventory Tracking Log will be kept for at least 5 years from the date of the final log entry.

1.3 Prescriber Requirements

Biogen Idec will accept registration of prescribers who agree to the following:

- To comply with the TOUCH™ program.
- To determine that a patient has a relapsing form of MS based on clinical and radiological evidence before prescribing TYSABRI®.
- That he/she is capable of diagnosing and managing opportunistic infections and PML, or prepared to refer to specialists with those abilities.
- To counsel all patients on the benefits and risks of TYSABRI® therapy, including the risks of PML, and to provide each patient with the TYSABRI® Medication Guide.
- To not prescribe TYSABRI® to any patient who is inappropriate for receiving the drug under the TOUCH™ program.
- To sign and complete the Prescriber/Patient Enrollment form for each patient, and to fax it to Biogen Idec before the patient can begin to receive infusions.
- To report to Biogen Idec, as soon as possible, any case of PML, any hospitalization due to opportunistic infection, and any death.
- To evaluate the patient 3 months after the first infusion, 6 months after the first infusion, every 6 months thereafter as long as the patient receives TYSABRI®, and 6 months after TYSABRI® has been discontinued.
- To determine every 6 months whether each patient should continue on TYSABRI® therapy and fill out the Patient Status Report and Reauthorization Questionnaire.

1.4 Patient Requirements

Biogen Idec will accept registration for patients who meet the following conditions:

- Must be registered in the TOUCH™ program.
- Must understand the risks and benefits of TYSABRI® treatment, including that taking the drug increases the risk of getting PML.
- Must complete and sign the Prescriber/Patient Enrollment Form indicating the patient's understanding of the potential risks associated with TYSABRI® treatment.
- Must agree to contact their prescriber if new or worsening symptoms, especially nervous system symptoms develop.
- Must read the TYSABRI® Medication Guide.
- Must agree to notify the TOUCH™ program if they switch infusion sites and/or prescribers
- Must provide information about other medicines and treatments at each TYSABRI® infusion.

2. Educational Program

Biogen Idec, Inc. will provide prescribers, infusion site staff, pharmacists and patients with educational materials on the benefits and risks associated with TYSABRI® therapy, the increased risk of PML, and the requirements of the TOUCH™ program.

2.1 Healthcare Provider and Patient Educational Materials

Educational information about the drug will be distributed to prescribers, pharmacies, infusion sites, and patients.

The TOUCH™ Educational Materials and forms include:

- The Patient Medication Guide and Package Insert (for patients and prescribers)
- TOUCH™ Prescribing Education Slide Set
- TYSABRI® and TOUCH™ Prescribing Program Slide Set (for prescribers and patients)
- TOUCH™ Prescribing Program Overview (general description)
- Prescriber/Patient Enrollment Form (signed by patients and prescribers)
- Infusion Site Enrollment Form (for infusion site enrollment)
- Central Pharmacy Enrollment Form (for central pharmacy enrollment into TOUCH™)
- TYSABRI® Inventory Tracking Log (central pharmacies use to document dispensing of TYSABRI® to affiliated authorized infusion sites)
- Patient Status Report and Reauthorization Questionnaire (filled out ever 6 months by prescribers)
- TYSABRI® Patient Discontinuation Notification Form (for prescribers to de-enroll a patient from the program)
- TYSABRI® Patient Discontinuation Questionnaire (for prescribers to complete at discontinuation and 6 months after the patient discontinues TYSABRI®)
- TOUCH™ Enrollment Kit (for prospective prescribers -- contains above information and describes program)
- Dear Doctor and Dear Patient Letters
- Patient Getting Started Brochure (information for patients about TOUCH™ and TYSABRI®)
- Healthcare Professional Infusion Guide (for infusion sites)
- Guidance for Evaluation of New Neurologic Symptoms in Patients Receiving TYSABRI® (for healthcare professionals)

2.2 Additional Information Sources

- www.TYSABRI.com
- Biogen Idec's Call Center: a call center designed to respond to healthcare provider, pharmacist, infusion center, and patient questions and requests for information.

3. Reporting: Biogen Idec, Inc. will implement a reporting and collection system for safety information as follows:

- All spontaneous and solicited adverse event reports from any post-marketing source will be reported as per 21 CFR 600.80.
- Within 15 calendar days a report for all confirmed cases of PML will be sent to FDA. Summary numbers for possible cases as flagged by the pre-infusion checklist will be reported in the periodic report.
- Within 15 calendar days a report of any other serious opportunistic infections or deaths of any cause will be reported to FDA.

Biogen Idec, Inc. will also establish a Pregnancy Registry in the US to determine the safety of TYSABRI® in pregnant patients. The primary objective will be to evaluate any pattern or increase in birth defects in children of women with MS who were exposed to TYSABRI® at any time within 3 months prior to conception, or at any time during pregnancy, where the outcome of the pregnancy is unknown at the time of enrollment.

4. TOUCH™ Safety Surveillance

Biogen Idec, through the TOUCH™ prescribing program will systematically follow and actively solicit information regarding the occurrence of PML and other serious opportunistic infections through a variety of mechanisms on every TYSABRI®-treated patient in the U.S. The various mechanisms include: through collection and assessment of Pre-Infusion Patient Checklists and the Prescriber/Patient Enrollment form; through serious adverse event reporting; and through contact with prescribers every 6 months in the form of a Patient Status Report and Reauthorization Questionnaire. In addition, attempts will be made to find and follow for 6 months patients who discontinue TYSABRI® treatment. Biogen Idec and Elan Pharmaceuticals are also creating a joint TYSABRI® Safety Review Committee to review safety data and determine any appropriate corrective actions, if needed.

5. TOUCH™ Program Evaluation

Biogen Idec, Inc. will evaluate the effectiveness of the TYSABRI® RiskMAP and will report the results quarterly for the first year, then every 6 months for 2 years, and annually thereafter to FDA. Each submission to FDA will include analyses of two major datasets:

- Health Outcomes Data (e.g. PML rate, overall safety)
- Systems/Process Data, Quality and Compliance Metrics

Biogen Idec, Inc. is also establishing a multi-disciplinary TYSABRI® Risk Management Review Committee to evaluate the effectiveness of the risk management plan. The decisions and outcomes of the Committee will be included in the TYSABRI® RiskMAP reports to FDA. In addition, Biogen Idec, Inc. and Elan Pharmaceuticals will create a joint TYSABRI® Compliance Review Committee to facilitate RiskMAP compliance.